HEPATITIS C
November 2004

1: AIDS Treat News. 2004 Jul 23(403):5.
Hepatitis coinfection: two major studies published. [No authors listed]
Two large trials showing successful treatment of hepatitis C in persons with HIV were published in the New England Journal of Medicine.
Publication Types:
Newspaper Article
PMID: 15386854 [PubMed - indexed for MEDLINE]

2: Am J Clin Pathol. 2004 Sep;122(3):428-33.
Carriage of the apolipoprotein E-epsilon4 allele and histologic outcome of recurrent hepatitis C after antiviral treatment.
Toniutto P, Fabris C, Fumo E, Apollonio L, Caldato M, Mariuzzi L, Avellini C, Minisini R, Pirisi M.
Department of Pathology and Medicine Experimental and Clinical, University of Udine, Italy.
Carriage of the epsilon4 allelic variant of the apolipoprotein E (ApoE) gene might affect the outcome of hepatitis C virus (HCV) infection. The liver transplantation setting offers the opportunity to verify the role of the donor's vs recipient's ApoE polymorphism. Twenty-four patients (16 men) with recurrent hepatitis C, all infected by HCV-1b and treated with interferon and ribavirin, were genotyped for ApoE variants. Liver biopsies were done at baseline and 12
months later After treatment, staging scores improved in 10 of 24 patients. Staging improvement was associated with recipient sex, completion of the full antiviral schedule, and recipient's epsilon4 carriage. The beneficial effect of epsilon4 carriage toward the progression of fibrosis was due entirely to the contribution given by male patients and was independent of the viral response. Recipients', but not donors', carriage of at least 1 epsilon4 allele might be associated with a better histologic outcome in recurrent HCV infection.
Publication Types:
Historical Article
PMID: 15362374 [PubMed - indexed for MEDLINE]

3: Am J Gastroenterol. 2004 Sep;99(9):1738-43.
Serum levels of hepatitis C virus core antigen as a marker of infection and response to therapy.
Soffredini R, Rumi MG, Parravicini ML, Ronchi G, Del Ninno E, Russo A, Colombo M.
A.M. Migliavacca Center for Liver Disease, Department of Gastroenterology and Endocrinology, IRCCS Maggiore Hospital and University of Milan, Via Pace 9, 20122 Milan, Italy.
OBJECTIVES: Hepatitis C virus (HCV) core antigen is a recently developed marker of hepatitis C infection. We compared the predictive power of HCV core antigen with reverse transcription polymerase chain reaction (RT-PCR) and branched DNA assay for HCV-RNA as markers of infection and response to interferon therapy. METHODS: Four hundred and forty-four sera from 111 patients (65 men, 52 yr) with chronic hepatitis C, receiving ribavirin together with standard interferon (n =61) or pegylated interferon (n = 50) were retrospectively investigated. RESULTS:
Pretreatment, RT-PCR, branched DNA (median 621,887 IU/ml), and HCV core antigen (median 57 pg/ml) gave positive results in 100%, 99%, and 94% of the sera; the correlation between HCV core antigen and branched DNA was 0.75. The median HCV RNA level among

the 7 of 111 (6%) patients that had a negative core Ag result was 15,016 IU/ml. Pretreatment levels of HCV core antigen were significantly lower in the 41 patients with a sustained virological response than in the 39 relapsers and 31 nonresponders (17 pg/ml, 114 pg/ml, 58 pg/ml; p-value 0.005). Independently of treatment schedule, wk 12 more than 2 log(10) reduction of
viremia or a negative result for HCV core antigen had 100% negative predictive value (NPV) for a response to therapy compared to 94% for negative RT-PCR. The positive predictive value (PPV) of HCV core antigen and branched DNA was only 47% and 48%. CONCLUSIONS: In conclusion, the HCV core antigen is a less sensitive test of HCV viremia than HCV-RNA assays and is competitive with the bDNA assay as an early predictor of a nonresponse.
PMID: 15330912 [PubMed - indexed for MEDLINE]

4: Am J Gastroenterol. 2004 Sep;99(9):1733-7.
Peginterferon alfa-2b plus ribavirin for the treatment of chronic hepatitis C genotype 4.
Hasan F, Asker H, Al-Khaldi J, Siddique I, Al-Ajmi M, Owaid S, Varghese R, Al-Nakib B.
Department of Medicine, Faculty of Medicine, Kuwait University, PO Box 24923, Safat 13110, Kuwait.
BACKGROUND: The hepatitis C virus (HCV) genotype is an important predictive parameter for the success of pegylated interferon plus ribavirin therapy. To date, most published therapeutic trials have enrolled patients infected mainly with HCV genotypes 1, 2, and 3. Data regarding the responsiveness of genotype 4, the predominant type of HCV in the Middle East, are very limited. OBJECTIVE: To assess the efficacy of peginterferon alfa-2b in combination with ribavirin for the treatment of chronic hepatitis caused by HCV genotype 4. METHODS: Sixty-six
treatment-naive patients infected with HCV genotype 4 were enrolled in this open label, prospective study. Cohort characteristics included the following: 48 M/18 F, mean age 45 +/- 9 years, and mean weight 74 +/- 8 kg. All patients had raised alanine aminotransferase (ALT) and were compensated. The mean pretreatment HCV-RNA level was 4.2 x 10(6) copies/ml (8.4 x 10(5) iu/ml) and median was 2.15 x 10(6) copies/ml. Twenty patients (29%) exhibited cirrhosis or severe fibrosis on pretreatment liver biopsy specimens. Participants were to receive
peginterferon alfa-2b, 1.5 mcg/kg/wk plus ribavirin 1,000-1,200 mg/day for 48 wk. Patients were followed up for 24 wk after completing therapy. End of treatment viral response and sustained viral response (SVR) were defined as the absence of HCV-RNA from serum (<100 copies/ml) at 48 wk of treatment and at the end of follow-up, respectively. Data were analyzed on an intention-to-treat basis. RESULTS: End of treatment and sustained virologic response were 77% and 68%, respectively. Among patients with pretreatment HCV-RNA > or =2 x 10(6) SVR
was 55% compared with SVR of 86% among patients with HCV-RNA < 2 x 10(6) (p=0.05). Patients with cirrhosis or severe fibrosis had significantly lower SVR rate compared to those with mild or no fibrosis (29 vs 84%; p < 0.0002). Three patients (4%) discontinued therapy because of severe flu-like symptoms. Four patients developed hypothyroidism. Dose reduction of ribavirin and peginterferon alfa-2b was necessary in 15% and 6% of the patients, respectively. CONCLUSION: Peginterferon alfa-2b in combination with ribavirin is effective in the treatment of HCV genotype 4. The treatment was well tolerated by most of the patients.
PMID: 15330911 [PubMed - indexed for MEDLINE]

5: Am J Gastroenterol. 2004 Sep;99(9):1720-5.

Hepatitis C knowledge among primary care residents: is our teaching adequate for the times?
Coppola AG, Karakousis PC, Metz DC, Go MF, Mhokashi M, Howden CW, Raufman JP, Sharma VK.
Division of Gastroenterology and Hepatology, University of Arkansas for Medical Sciences, Little Rock, AR, USA.
BACKGROUND: Increasingly, primary care (PC) physicians will be the first to encounter patients with hepatitis C virus (HCV) infection. AIM: To determine opinions and practices of PC residents regarding HCV. METHODS: We administered a one-page questionnaire to 180 PC residents at five U.S. training programs. RESULTS: Respondents were distributed equally across postgraduate year, 83% were U.S. graduates, and 44% had seen >11 (HCV) patients in the past year. Residents tested for HCV in persons with: increased transaminases (83%),

history of blood transfusion (46%), multiple tattoos (57%), +ANCA (16%), and alcohol abuse (31%). Sixteen percent of respondents tested all patients. Forty-one percent would vaccinate HCV patients for hepatitis A and 65% for hepatitis B while only 19% and 78% knew the respective vaccination schedules. Although no vaccine is available, 66% recommended vaccination for HCV. Only 37% and 29%, respectively, reported HCV genotype 1 as most common and most resistant to treatment. Fifty-three percent recommend liver biopsy before treating HCV. Only 52% reported alpha-interferon (IFN) with ribavirin as initial treatment for HCV
while 28% recommend ribavirin or lamivudine alone or combinations of IFN and lamivudine or amantadine. As contraindications to treatment, 33% reported AIDS with PCP infection, 19% coronary artery disease, and 19% suicidal ideation. Sixty-nine percent felt that there was insufficient information on HCV. CONCLUSIONS: Many PC residents lack adequate knowledge of recommended guidelines for the management of HCV. Many test for HCV in inappropriate situations, are unclear regarding available vaccines and their administration, and are uncertain about current treatment. Education of PC residents on guidelines for detection and management of HCV must be improved.
PMID: 15330909 [PubMed - indexed for MEDLINE]

6: Am J Gastroenterol. 2004 Sep;99(9):1706-7.
Comment on:
Am J Gastroenterol. 2004 Sep;99(9):1700-5.
Chronic hepatitis C and normal ALT: considerations for treatment.
Bacon BR.
Improvements in the treatment of patients with chronic hepatitis C have progressed over the past 14 yr. Initially, treatment of patients with persistently normal ALT levels was not considered necessary. As treatment response improved, more of these patients were treated. Jacobson and colleagues have shown that patients with normal ALT levels respond similarly to those with
elevated ALT levels when treated with the combination of interferon and ribavirin. ALT levels are a poor marker of disease severity and/or indication for treatment in patients with chronic hepatitis C.
Publication Types:
Comment
Editorial
PMID: 15330906 [PubMed - indexed for MEDLINE]

7: Am J Gastroenterol. 2004 Sep;99(9):1700-5.
Comment in:
Am J Gastroenterol. 2004 Sep;99(9):1706-7.
Interferon alpha-2b and ribavirin for patients with chronic hepatitis C and normal ALT.
Jacobson IM, Ahmed F, Russo MW, Lebovics E, Dieterich DT, Esposito SP, Bach N, Klion F, Tobias H, Antignano L, Brown RS Jr, Gabbaizadeh D, Geders J, Levendoglu H.
Department of Gastroenterology and Hepatology, Weill Medical School of Cornell University, 450 East 69th Street, New York, NY 10021, USA.
OBJECTIVES: Most studies establishing the role of antiviral therapy in patients with chronic hepatitis C (CHC) excluded the patients with normal ALT levels. Small trials with interferon monotherapy suggested a limited efficacy and/or de novo ALT elevations. We sought to evaluate the efficacy of two doses of interferon alpha-2b (IFN) with ribavirin (RBV) in patients with normal ALT. METHODS: Patients with biopsy-proven CHC with detectable HCV RNA and at least two normal ALT levels three or more months apart were randomized to receive
either 3 or 5 million units of IFN thrice a week plus RBV 1,000-1,200 mg. Therapy was stopped at 24 wk if HCV RNA remained detectable and continued for an additional 24 wk if HCV RNA was undetectable. A final HCV RNA level was obtained 24 wk after discontinuation of therapy. RESULTS: Fifty-six patients were randomized and received at least one dose of treatment. The overall rate of sustained virologic response (SVR) was 32%. SVR rates were higher in genotype 2 and 3 patients (80%) than in genotype 1 patients (24%, p = 0.002). There was a tendency toward higher SVR in genotype 1 patients treated with the higher IFN dose (36%vs 10%, p = 0.07). Five patients had mild, transient ALT elevations. No sustained ALT elevations were noted. CONCLUSIONS: Patients with normal ALT had a rate of SVR comparable to that reported in patients with elevated ALT. Higher dose of interferon tended to be more effective in genotype 1 infected patients. De novo ALT elevations were transient and

not clinically significant. Patients with CHC should not be excluded from treatment on the basis of ALT alone.
Combination therapy with pegylated interferon and ribavirin should be evaluated in these patients.
Publication Types:
Clinical Trial
Multicenter Study
Randomized Controlled Trial
PMID: 15330905 [PubMed - indexed for MEDLINE]

8: Am J Gastroenterol. 2004 Aug;99(8):1517-22.
Estimating the date of hepatitis C virus infection from patient interviews and antibody tests on stored sera.
Bruden DL, McMahon BJ, Hennessy TW, Christensen CJ, Homan CE, Williams JL, Sullivan DG, Gretch DR, Cagle HH, Bulkow LR.
Arctic Investigations Program, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Anchorage, Alaska 99508, USA.
OBJECTIVES: Studies on the natural history and outcome of chronic hepatitis C virus (HCV) infection differ regarding the proportion of persons who develop serious sequelae over time. Most of these studies use an estimated date of HCV infection based on risk factor data obtained from patient interviews. The date of HCV infection is often estimated using the year of a pre-1992 blood transfusion (BT), or the first year of injecting drug use (IDU). We sought to
determine the accuracy of these dates obtained by interview. METHODS: We compared BT dates reported by patients in a long-term HCV outcome study to dates confirmed in a BT-Lookback project, and also compared the reported first year of IDU to seroconversion dates estimated from HCV tests on historical sera. RESULTS: Of 28 BT recipients who were interviewed in the HCV outcome study and identified in the Lookback project, 14 (50%; 95% CI: 31-69%) were unaware they had received a BT. Of 25 persons identified in the BT-Lookback project with historical sera available, 9 (36%; 95% CI: 19-57%) had anti-HCV results that did
not correlate with their confirmed BT date. Of 216 persons with a history of IDU and historical serum samples available, 66 (31%; 95% CI: 25-37%) had anti-HCV results that did not correlate with their reported first year of IDU. CONCLUSIONS: Inaccuracies in the length of HCV could occur in outcome studies that rely on patient recall of risk-factor history. Statistical methods that
incorporate the uncertainty in assigning infection date are needed. Copyright 2004 American College of Gastroenterology
PMID: 15307870 [PubMed - indexed for MEDLINE]

9: Am J Gastroenterol. 2004 Aug;99(8):1490-6.
Cost-effectiveness of combination peginterferon alpha-2a and ribavirin compared with interferon alpha-2b and ribavirin in patients with chronic hepatitis C.
Sullivan SD, Jensen DM, Bernstein DE, Hassanein TI, Foster GR, Lee SS, Cheinquer H, Craxi A, Cooksley G, Klaskala W, Pettit K, Patel KK, Green J.
University of Washington, Seattle WA 98195, USA.
BACKGROUND: Sustained virological response (SVR) is the primary objective in the treatment of chronic hepatitis C (CHC). Results from a recent clinical trial of patients with previously untreated CHC demonstrate that the combination of peginterferon alpha-2a and ribavirin produces a greater SVR than interferon alpha-2b and ribavirin combination therapy. However, the cost-effectiveness of peginterferon alpha-2a plus ribavirin in the U.S. setting has not been investigated. METHODS: A Markov model was developed to investigate cost-effectiveness in patients with CHC using genotype to guide treatment duration. SVR and disease progression parameters were derived from the clinical trials and epidemiologic studies. The impact of treatment on life expectancy and costs were projected for a lifetime. Patients who had an SVR were assumed to remain virus-free for the rest of their lives. In genotype 1 patients, the SVRs were 46% for peginterferon alpha-2a plus ribavirin and 36% for interferon alpha-2b plus ribavirin. In genotype 2/3 patients, the SVRs were 76% for peginterferon alpha-2a plus ribavirin and 61% for interferon alpha-2b plus ribavirin. Quality of life and costs were based on estimates from the literature. All costs were based on published U.S. medical care costs and were

adjusted to 2003 U.S. dollars. Costs and benefits beyond the first year were discounted at 3%. RESULTS: In genotype 1, peginterferon alpha-2a plus ribavirin increases quality-adjusted life expectancy (QALY) by 0.70 yr compared to interferon alpha-2b plus ribavirin, producing a cost-effectiveness ratio of $2,600 per QALY gained. In genotype 2/3 patients, peginterferon alpha-2a plus ribavirin increases QALY by 1.05 yr in comparison to interferon alpha-2b plus ribavirin. Peginterferon alpha-2a combination therapy in patients with HCV genotype 2 or 3 is dominant (more effective and cost saving) compared to interferon alpha-2b plus ribavirin. Results weighted by genotype prevalence (75% genotype 1; 25% genotype 2 or 3) also show that peginterferon alpha-2a plus ribavirin is dominant. Peginterferon alpha-2a and ribavirin remained
cost-effective (below $16,500 per QALY gained) under sensitivity analyses on key clinical and cost parameters. CONCLUSION: Peginterferon alpha-2a in combination with ribavirin with duration of therapy based on genotype, is cost-effective compared with conventional interferon alpha-2b in combination with ribavirin when given to treatment-naÃ¯ve adults with CHC. Copyright 2004 American College of Gastroenterology
PMID: 15307866 [PubMed - indexed for MEDLINE]

10: Am J Med. 2004 Sep 1;117(5):344-52.
Hepatitis C treatment update.
Pearlman BL.
Center For Hepatitis C, Atlanta Medical Center, Atlanta, Georgia 30312, USA. brianpearlman@hotmail.com
Hepatitis C is a leading cause of chronic liver disease in the United States, and the prevalence of hepatitis C-associated complications is increasing. Therapy with pegylated interferon and ribavirin has become the standard of care for chronic hepatitis C; the sustained response rate for treatment-naÃ¯ve patients is about 55%. If certain patients fail to achieve a 12-week treatment milestone, an early virologic response, they may be taken off treatment early, potentially sparing them from unnecessary medication. Adherence is critical for treatment success. Although side effects continue to be a hindrance to the success of therapy, agents such as growth factors and antidepressants may help patients to maintain medication dosing and complete treatment. Therapy is generally recommended for those in whom the infection is most likely to progress to cirrhosis; however, there is continued debate about the suitability of certain patients for treatment, including those with persistently normal aminotransferase levels or acute hepatitis C and nonresponders to conventional treatment. Four broad groups of investigational therapeutic agents appear promising for future therapy: modified interferons and ribavirins, immunomodulators, viral life-cycle targets, and antifibrotic agents.
Publication Types:
Review
Review, Tutorial
PMID: 15336584 [PubMed - indexed for MEDLINE]

11: Am J Trop Med Hyg. 2004 Aug;71(2):153-9.
Human immunodeficiency virus type 1 and other viral co-infections among young heterosexual men and women in Argentina.
de los Angeles Pando M, Biglione MM, Toscano MF, Rey JA, Russell KL, Negrete M, Gianni S, Martinez-Peralta L, Salomon H, Sosa-Estani S, Montano SM, Olson JG, Sanchez JL, Carr JK, Avila MM.
Centro Nacional de Referencia para el SIDA, Buenos Aires, Argentina. mpando@fmed.uba.ar
Infections with hepatitis C virus, (HCV), hepatitis B virus (HBV), and human T lymphotropic type I/II (HTLV-I/II) virus are commonly found in patients infected with human immunodeficiency virus type 1 (HIV-1). We conducted a seroepidemiologic study among 174 HIV-positive heterosexuals in Buenos Aires, Argentina in 1999. Evidence of exposure to HCV, HBV, and HTLV-I/II was found in 32%, 17%, and 5%, respectively. A higher prevalence of HBV infection was observed among males (33%) compared with females (12%; $P < 0.05$). Among women, a prior history of a sexually transmitted infection, injecting drug use (IDU), having had more than five lifetime sex partners, and having exchanged sex-for-goods were significantly associated with HCV infection, whereas an IDU history, syringe sharing, and having exchanged sex-for-goods were found to be
associated with HBV infection. Among men, an IDU history and syringe/needle sharing were significantly associated with HCV infection. The IDU-related and sexual transmission of hepatitis viruses constitute a significant problem among young, HIV-infected, heterosexuals in Argentina.

PMID: 15306703 [PubMed - indexed for MEDLINE]

12: BMJ. 2004 Sep 25;329(7468):733-6.
Taking account of future technology in cost effectiveness analysis.
Salomon JA, Weinstein MC, Goldie SJ.
Department of Population and International Health, Harvard School of Public Health, Harvard Center for Population and Development Studies, 9 Bow Street, Cambridge MA 02138, USA. jsalomon@hsph.harvard.edu
Publication Types:
Review
Review, Tutorial
PMID: 15388618 [PubMed - indexed for MEDLINE]

13: Clin Exp Immunol. 2004 Aug;137(2):417-23.
Isolation and functional analysis of circulating dendritic cells from hepatitis C virus (HCV) RNA-positive and HCV RNA-negative patients with chronic hepatitis C: role of antiviral therapy.
Tsubouchi E, Akbar SM, Murakami H, Horiike N, Onji M.
Third Department of Internal Medicine, Ehime University School of Medicine, Ehime, Japan.
Hepatitis C virus (HCV) RNA has been localized in antigen-presenting dendritic cells (DCs) from patients with chronic hepatitis C (CHC). DCs from patients with CHC also exhibit impaired functional capacities. However, HCV RNA in DCs and functional impairment of DCs in CHC might be independent or interrelated events. Moreover, the impact of antiviral therapy on the functions of DCs in CHC is not well documented. In order to address these issues, we took advantage of antiviral therapy in these patients. Ten patients with CHC, expressing HCV RNA in circulating DCs, became negative for HCV RNA in circulating DCs after therapy with interferon-alpha and ribavirin for 4 weeks. The functions of DCs from HCV RNA+ patients (isolated before antiviral therapy) and HCV RNA- patients (isolated 4 weeks after antiviral therapy) were compared in allogenic mixed leucocyte reactions. In comparison to circulating DCs from normal control subjects, DCs from HCV RNA+ patients had a significantly decreased capacity to stimulate allogenic T lymphocytes ($P < 0.01$) and produce interleukin-12 ($P < 0.05$). However, the allostimulatory capacity of circulating DCs from HCV RNA-patients was several-fold higher compared to that of HCV RNA+ DCs from the same patient. DC from HCV RNA- patients also produced significantly higher levels of interleukin-12 compared to HCV RNA+ DCs from the same patient ($P < 0.01$). Taken together, this study is the first to provide experimental evidence regarding the impact of HCV RNA and antiviral therapy on the function of DCs in patients with CHC.
PMID: 15270861 [PubMed - indexed for MEDLINE]

14: Clin Exp Immunol. 2004 Aug;137(2):408-16.
CD56(+dim) and CD56(+bright) cell activation and apoptosis in hepatitis C virus infection.
Lin AW, Gonzalez SA, Cunningham-Rundles S, Dorante G, Marshall S, Tignor A, Ha C, Jacobson IM, Talal AH.
Center for the Study of Hepatitis C, Department of Medicine, Weill Medical College of Cornell University, New York 10021, USA.
CD3- CD56(+dim) natural killer (NK) cells, which are cytotoxic against virally infected cells, may be important in hepatitis C virus (HCV)-infected patients who are successfully treated with pegylated interferon (PEG-IFN)-alpha. We used flow cytometry to enumerate activated (CD69+) and apoptotic (annexin-V+) dim (CD3- CD56(+dim)) and bright (CD3- CD56(+bright)) NK cells obtained from HCV-infected patients before treatment (n=16) and healthy controls (n=15) in the
absence and presence of pegylated interferon (PEG-IFN)-alpha-2b. A subset of HCV-infected patients, subsequently treated with PEG-IFN-alpha-2b in vivo, was determined to have a sustained virological response (SVR, n=6) or to not respond (NR) to treatment (n=5). In the absence of IFN, activated dim (CD3- CD56(+dim) CD69+) NK cells were significantly decreased (P=0.04) while activated apoptotic dim (CD3- CD56(+dim)CD69+ annexin-V+) NK cells tended to be increased (P=0.07) in SVR patients compared with NR patients. Activated bright
(CD3-CD56(+bright)CD69+) and activated apoptotic bright (CD3- CD56(+bright)CD69+ annexin-V+) NK cells were significantly correlated (P=0.02 and P=0.01, respectively) with increasing hepatic inflammation. These findings suggest that in the absence of PEG-IFN, activated dim (CD3- CD56(+dim)CD69+) NK cell turnover may be enhanced in SVR compared

with NR patients and that activated bright (CD3-CD56(+bright)CD69+) NK cells may play a role in liver inflammation.
PMID: 15270860 [PubMed - indexed for MEDLINE]

15: Curr Opin Drug Discov Devel. 2004 Jul;7(4):446-59.
Progress and development of small molecule HCV antivirals.
Ni ZJ, Wagman AS.
Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608, USA. zhi-jie_ni@chiron.com
Hepatitis C virus (HCV) is a disease that has a growing impact worldwide. A combination therapy comprising interferon-alpha (IFNalpha) and ribavirin represents the current standard treatment for chronic HCV infection, although it has demonstrated limited success and causes some serious side effects. Promising alternative approaches toward the control of HCV infection, and the development of new antiviral agents, include the use of NS3/4A serine protease and NS5B polymerase inhibitors. Successful proof-of-concept clinical trials of the NS3/4A protease inhibitor BILN-2061 have confirmed the usefulness of a peptidomimetic product-based approach, providing impetus for the generation of improved molecules. Preclinical results from the development of HCV polymerase inhibitors, both nucleoside and non-nucleoside, are promising. This review provides an overview of recent progress in these areas, and discusses the potential of various approaches toward small molecule HCV antivirals.
Publication Types:
Review
Review, Tutorial
PMID: 15338954 [PubMed - indexed for MEDLINE]

16: Dig Liver Dis. 2004 Aug;36(8):547-50.
Reported risk factors are useless in detecting HCV-positive subjects in the general population.
Stroffolini T, Mariano A, Iantosca G.
Laboratory of Epidemiology, Istituto Superiore di Sanita (ISS), Vale Regina Elena 299, 00161 Rome, Italy. iantosca@iss.it
BACKGROUND: Chronic hepatitis C virus infection is mostly asymptomatic, so it will not be identified if specific diagnostic tests are not performed. AIMS: To evaluate the positive predictive value of some risk factors in detecting anti-hepatitis C virus-positive subjects in the general population. SUBJECTS: Two-thousand five hundred and sixty-one subjects randomly selected from the list of the census in three population-based surveys performed in hepatitis C virus
endemic areas in Southern Italy. METHODS: The sensitivity, specificity and positive predictive value of blood transfusion, past use of glass syringes and surgical intervention in detecting hepatitis C virus positivity were assessed. Data were collected using a precoded questionnaire administered by an interviewer. RESULTS: All risk factors showed a poor positive predictive value (ranging from 21.0% for surgical intervention to 29.0% for blood transfusion). The positive predictive value was extremely low (ranging from 2.9 to 4.3%) in subjects younger than 46 years of age, who mostly could benefit from antiviral treatment. The combination of the simultaneous presence of more than one risk factor does not improve the detection of hepatitis C virus infection. CONCLUSIONS: Reported risk factors are useless in detecting hepatitis C virus-positive subjects in the general population.
Publication Types:
Clinical Trial
Randomized Controlled Trial
PMID: 15334776 [PubMed - indexed for MEDLINE]

17: Eur J Gastroenterol Hepatol. 2004 Sep;16(9):933-6.
Spontaneous regression of hepatocellular carcinoma: report of a case.
Feo CF, Marrosu A, Scanu AM, Ginesu GC, Fancellu A, Migaleddu V, Porcu A.
Department of Surgery, Institute of Clinica Chirurgica, Italy. cffeo@uniss.it
The widespread use of ultrasound in screening programmes for chronic liver disease has led to early diagnosis of hepatocellular carcinoma (HCC), and to the observation of some cases of tumour spontaneous regression. This is a rare event whose underlying mechanism is still unclear. We present here a case of spontaneous regression of HCC in a 71-year-old woman with chronic hepatitis and discuss possible aetiologies. None of the causative mechanisms proposed for spontaneous regression of HCC is completely satisfactory, so further studies are

necessary to improve understanding of this unusual biological event. Therefore, we stress the importance of accumulating all such cases in the literature, because the clarification of aetio-pathogenic mechanisms may lead to the development of new treatment strategies for HCC.
Publication Types:
Case Reports
PMID: 15316421 [PubMed - indexed for MEDLINE]

18: Eur J Gastroenterol Hepatol. 2004 Sep;16(9):891-6.
Correlation of serum aminotransferases with HCV RNA levels and histological findings in patients with chronic hepatitis C: the role of serum aspartate transaminase in the evaluation of disease progression.
Zechini B, Pasquazzi C, Aceti A.
Department of Infectious Diseases, Sant'Andrea Hospital, University of Rome La Sapienza, Italy.
OBJECTIVES: To investigate whether HCV RNA levels can be considered to be predictors of hepatocellular injury in patients with chronic hepatitis C, and whether aminotransferase levels are markers of liver damage. METHODS: We performed a retrospective study on 112 patients with chronic hepatitis C. For each patient, we considered the baseline alanine aminotransferase (ALT) and serum aspartate transaminase (AST) levels, baseline HCV RNA, HCV genotype,
histological evaluation and the mean aminotransferase levels measured in the 6 months following liver biopsy. RESULTS: We found a statistically significant correlation between HCV RNA and aminotransferase levels measured during the follow-up (AST: r = 0.24, P = 0.01; ALT: r = 0.27, P = 0.004). We also observed a statistically significant correlation between HCV RNA levels and histological activity index (HAI) (r = 0.25, P = 0.008), as well as between the HAI and both baseline AST (r = 0.34, P = 0.0002) and ALT levels (r = 0.23, P = 0.01). These findings were confirmed by the mean aminotransferase values during follow-up. In the regression analysis, the fibrosis score was significantly and independently associated with baseline AST and ALT values. CONCLUSIONS: Our results demonstrate a statistically significant correlation of aminotransferase values with the histological parameters, and an even stronger correlation with the AST values. Our study therefore suggests that aminotransferase values, especially
AST, may correlate with liver damage.
Publication Types:
Evaluation Studies
PMID: 15316414 [PubMed - indexed for MEDLINE]

19: Gut. 2004 Sep;53(9):1388.
Improving hepatitis C services across the UK: response to a walk-in HCV testing service.
D'Souza RF, Glynn MJ, Alstead E, Foster GR, Ushiro-Lumb I.
Publication Types:
Letter
PMID: 15306607 [PubMed - indexed for MEDLINE]

20: Gut. 2004 Sep;53(9):1345-51.
Sustained virological response in hepatitis C virus type 1b infected patients is predicted by the number of mutations within the NS5A-ISDR: a meta-analysis focused on geographical differences.
Pascu M, Martus P, Hohne M, Wiedenmann B, Hopf U, Schreier E, Berg T.
Medizinische Klinik m S Hepatologie und Gastroenterologie, Charite, Universitatsmedizin Berlin, Campus Virchow-Klinikum, Augustenburger Platz 1, 13353 Berlin, Germany. maria.pascu@charite.de
BACKGROUND AND AIMS: There is growing evidence that the response of hepatitis C virus (HCV) genotype 1b infected patients towards interferon (IFN) therapy is influenced by the number of mutations within the carboxy terminal region of the NS5A gene, the interferon sensitivity determining region (ISDR). PATIENTS AND METHODS: In order to attain better insight into this correlation, a file comprising published data on ISDR strains from 1230 HCV genotype 1b infected patients, mainly from Japan and Europe, was constructed and analysed by logistic regression. Sustained virological response (SVR) was defined as negative HCV RNA six months after treatment. RESULTS: The distribution of wild-, intermediate-, and mutant-type ISDR sequences differed significantly between Japanese (n = 655) (44.1%, 37.6%, and 18.3%) and European patients (n = 525) (24.8%, 63.4%, and 11.8%; p<0.001). There was a

significant positive correlation between the number of ISDR mutations and SVR rate, irrespective of geographical region. The likelihood of SVR with each additional mutation within the ISDR was considerably more pronounced in Japanese compared with European patients (odds ratios 1.82 v 1.39; p<0.001). Pretreatment viraemia of <6.6 log copies/ml and ISDR mutant-type infection was associated with an SVR rate of 97.1% in Japanese patients but only 52.5% in European patients. Pretreatment viraemia was a stronger predictor of SVR than ISDR mutation number in Japanese patients whereas in European patients both parameters had similar predictive power. CONCLUSION: These data support the concept that mutant-type ISDR strains may represent a subtype within genotype 1b with a more favourable response towards IFN therapy.
Publication Types:
Meta-Analysis
Review
Review, Academic
PMID: 15306598 [PubMed - indexed for MEDLINE]

21: Hepatogastroenterology. 2004 Sep-Oct;51(59):1476-9.
Successful application of highly purified natural interferon alpha (multiferon) in a chronic hepatitis C patient resistant to preceding treatment approaches.
Musch E, Malek M, von Eick H, Chrissafidou A.
Department of General Internal Medicine, Marienhospital Bottrop gGmbH, Germany. eugen.musch@mhb-bottrop.de
A currently 65-year-old patient with histologically proven chronic hepatitis C and chronic hepatitis B (seroconversion in 1990) and additional compensated cirrhosis of the liver (Child A) achieved sustained complete biochemical and viral response following 5 and 14 months respectively of therapy with highly purified natural leukocyte interferon-alpha (3 x 3 MU weekly, nIFN-alpha, Multiferon). Prior to this treatment, various other therapy approaches including
recombinant interferon-alpha2b (rIFN-alpha2b) or a combination of natural interferon-beta (nIFN-beta) and interferon-gamma (rIFN-gamma) had been carried out. Unfortunately, these had been unsuccessful. After a total treatment period of 76 months with nIFN-alpha and a subsequent follow-up period of 30 months, no relapse of chronic hepatitis C occurred. The patient's tolerance of the treatment was excellent and no substantial drug-related adverse events were observed. nIFN-alpha, which - unlike the recombinant IFN-alpha2 preparations - is a mixture of various physiologically expressed IFN-alpha subtypes, could possibly be an alternative in the treatment of difficult-to-treat patients with chronic hepatitis C.
Publication Types:
Case Reports
PMID: 15362781 [PubMed - indexed for MEDLINE]

22: Hepatogastroenterology. 2004 Sep-Oct;51(59):1417-21.
Inhibition of activated blood platelets by interferon alpha 2b in chronic hepatitis C.
Panasiuk A, Prokopowicz D, Zak J, Panasiuk B, Wysocka J.
Department of Infectious Diseases, Medical University of Bialystok, Bialystok, Poland. apanasiuk@wp.pl
BACKGROUND/AIMS: Interferon alpha used in treatment of chronic hepatitis C significantly influences the blood platelets. The role of platelets in initiating and developing pathological processes in hepatic diseases is still barely known. We studied the effects of interferon alpha 2b (IFN alpha2b) on blood platelets in chronic hepatitis C. METHODOLOGY: The studies were conducted in 16 patients who underwent IFN alpha2b treatment 3 times a week at 6MU. The examination was carried out before and on the 14th day of the treatment of IFN alpha2b. Morphological parameters of blood platelets were determined by hematological methods and flow cytometry. Expression of receptors on blood platelet surfaces (CD41, CD42a, CD62P) and thrombopoietin, platelet-derived growth factor, soluble form sP-selectin, IL-6, and tumor necrosis factor alpha were also determined. RESULTS: The use of IFN alpha2b in patients with chronic hepatitis C significantly effects blood platelets morphology by causing the decrease in their number, the change in population size, and the increase in large platelet count. Interferon decreases P-selectin expression on platelets, sP-selectin and platelet-derived growth factor concentration in plasma. During interferon therapy we noted increase concentration of thrombopoietin, tumor necrosis factor alpha, IL-6 in chronic hepatitis C. CONCLUSIONS: IFN alpha2b stabilizes activated platelets and probably decreases their participation in

inflammatory and fibrotic processes in the liver.
PMID: 15362767 [PubMed - indexed for MEDLINE]

23: Hepatology. 2004 Sep;40(3):760-1; author reply 761.
Comment on:
Hepatology. 2004 Jun;39(6):1702-8.
Peginterferon alfa-2a (40 kd) and ribavirin for black American patients with chronic HCV genotype 1.
Pijak MR, Gazdik F, Hrusovsky S.
Publication Types:
Comment
Letter
PMID: 15349918 [PubMed - indexed for MEDLINE]

24: Hepatology. 2004 Sep;40(3):756-8.
Reexamining the role of the humoral immune response in control of hepatitis C virus infection.
Dustin LB.
Center for the Study of Hepatitis C, The Rockefeller University, New York, NY, USA.
PMID: 15349916 [PubMed - indexed for MEDLINE]

25: Hepatology. 2004 Sep;40(3):708-18.
Hepatitis C virus NS5A-regulated gene expression and signaling revealed via microarray and comparative promoter analyses.
Girard S, Vossman E, Misek DE, Podevin P, Hanash S, Brechot C, Beretta L.
Department of Microbiology, University of Michigan, Ann Arbor, MI, USA.
Most individuals exposed to hepatitis C virus (HCV) become chronically infected and are predisposed to liver disease. The mechanisms underlying viral persistence and disease progression are unknown. A role for the HCV NS5A protein in viral replication and interferon resistance has been demonstrated. To identify mechanisms affected by NS5A, we analyzed the gene expression of Huh7 cells expressing NS5A and control cells using oligonucleotide microarrays. A set of 103 genes (43 up-regulated, 60 down-regulated) whose expression was modified by at least twofold was selected. These included genes involved in cell adhesion and motility, calcium homeostasis, lipid transport and metabolism, and genes regulating immune responses. The finding of modulated expression of genes related to the TGF-beta superfamily and liver fibrosis was observed. Interestingly, both the tumor necrosis factor and lymphotoxin beta receptors were down-regulated by NS5A. Similar data were obtained following expression of four NS5A mutants obtained from patients who were not responsive or were sensitive to interferon therapy. Through computational analysis, we determined that 39 of the 43 genes up-regulated by NS5A contained one or more nuclear factor kappaB (NF-kappaB) binding sites within their promoter region. Using the Gibbs sampling method, we also detected enrichment of NF-kappaB consensus binding sites in the upstream regions of the 43 coexpressed genes. Activation of NF-kappaB by NS5A was subsequently demonstrated in luciferase reporter assays. Adenovirus-mediated expression of IkappaBalpha reverted NS5A mediated
up-regulation of gene expression. In conclusion, this study suggests a role of NS5A and NF-kappaB in HCV pathogenesis and related liver disease. Supplementary material for this article can be found on the HEPATOLOGY website (http://interscience.wiley.com/jpages/0270-9139/suppmat/index.html). Copyright 2004 American Association for the Study of Liver Diseases
PMID: 15349911 [PubMed - indexed for MEDLINE]

26: Hepatology. 2004 Sep;40(3):699-707.
Comment in:
Hepatology. 2004 Sep;40(3):524-6.
Hepatitis C recurrence is more severe after living donor compared to cadaveric liver transplantation.
Garcia-Retortillo M, Forns X, Llovet JM, Navasa M, Feliu A, Massaguer A, Bruguera M, Fuster J, Garcia-Valdecasas JC, Rimola A.
Liver Unit, Hospital Clinic, Institut de Malalties Digestives, Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Barcelona, Spain.
Preliminary reports suggested that hepatitis C virus (HCV) infection has a more aggressive course following living donor liver transplantation (LDLT) compared to cadaveric liver

transplantation (CLT). The aim of this prospective study was to establish if HCV disease recurrence differs between LDLT and CLT. A cohort of 116 consecutive HCV-infected patients undergoing 117 LTs in a single center from March 2000 to August 2003 were followed-up, including systematic liver biopsies. Severe recurrence (SR) was defined as biopsy-proven cirrhosis and/or the occurrence of clinical decompensation. After a median follow-up of 22 months (2.6-44 months), 26 (22%) patients developed SR (decompensation in 12), involving 17 (18%) of 95 patients undergoing CLT and 9 (41%) of 22 undergoing LDLT. The 2-year probability of presenting SR was significantly higher in LDLT compared to CLT (45% vs. 22%, P = .019). By univariate analysis LDLT (P = .019) and an ALT higher than 80 IU/L 3 months after LT (P = .022) were predictors of SR. In 93 patients from whom a liver biopsy was available 3 months after LT, a lobular necroinflammatory score >1 (P < .01), LDLT (P < .01), and biliary
complications (P = .046) were associated with SR. However, the only variables independently associated with SR were LDLT (odds ratio [OR], = 2.8; 95% CI,1.19-6.6; P = .024) and a lobular necroinflammatory score > 1 (OR, 3.1; 95% CI, 1.2-8; P = .013). In conclusion, HCV recurrence is more severe in LDLT compared to CLT. Although our results were based on a single-center experience, they should be considered in the decision-making process of transplant programs,
since severe HCV recurrence may ultimately compromise graft and patient survival. Copyright 2004 American Association for the Study of Liver Diseases
PMID: 15349910 [PubMed - indexed for MEDLINE]

27: Hepatology. 2004 Sep;40(3):524-6.
Comment on:
Hepatology. 2004 Sep;40(3):699-707.
Is severe recurrent hepatitis C more common after adult living donor liver transplantation?
Russo MW, Shrestha R.
Publication Types:
Comment
Editorial
PMID: 15349889 [PubMed - indexed for MEDLINE]

28: Hepatology. 2004 Sep;40(3):516-9.
Hepatitis C infection and injection drug use: the role of hepatologists in evolving treatment efforts.
Kresina TF, Seeff LB, Francis H.
Center on AIDS and other Medical Consequences of Drug Abuse, National Institute on Drug Abuse, Department of Health and Human Services, Bethesda, MD 20892, USA. tk13v@nih.gov
Treatment regimens for both substance abuse and hepatitis C infection are complex and evolving. New pharmacotherapy for opioid addiction allows for office-based treatment and, thus, an opportunity for expanded treatment in the context of hepatitis C infection. The current article addresses the newly evolving, complex issues in the medical management of hepatitis C and injection drug use. Copyright 2004 American Association for the Study of Liver Diseases
PMID: 15349886 [PubMed - indexed for MEDLINE]

29: Hepatology. 2004 Aug;40(2):498.
Comment on:
Hepatology. 2004 Apr;39(4):1147-71.
Treatment of HCV infection in patients with advanced cirrhosis.
Forns X, Navasa M, Rodes J.
Publication Types:
Comment
Letter
PMID: 15368458 [PubMed - indexed for MEDLINE]

30: Hepatology. 2004 Aug;40(2):459-66.
Keratin 8 and 18 hyperphosphorylation is a marker of progression of human liver disease.
Toivola DM, Ku NO, Resurreccion EZ, Nelson DR, Wright TL, Omary MB.
Department of Medicine, Palo Alto VA Medical Center, Stanford University School of Medicine Digestive Disease Center, Palo Alto, CA 94304, USA. dtoivola@stanford.edu

Keratin 8 and 18 (K8/18) phosphorylation plays a significant and site-specific role in regulating keratin filament organization, association with binding proteins, and modulation of cell cycle progression. Keratin hyperphosphorylation correlates with exposure to a variety of stresses in cultured cells and in mouse models of liver, pancreatic, and gallbladder injury, and it is found in
association with mouse and human Mallory bodies. We asked whether K8/18 phosphorylation correlates with human liver disease progression by analyzing liver explants and biopsies of patients with chronic noncirrhotic hepatitis C virus (HCV) or cirrhosis. We also examined the effect of HCV therapy with interleukin-10 on keratin phosphorylation. Using site-specific antiphosphokeratin antibodies we found keratin hyperphosphorylation on most K8/18 sites in all cirrhotic liver explants tested and in most liver biopsies from patients with chronic HCV infection. Immunofluorescence staining of precirrhotic HCV livers showed focal keratin hyperphosphorylation and limited reorganization of keratin filament networks. In cirrhotic livers, keratin hyperphosphorylation occurred preferentially in hepatic nodule cells adjacent to bridging fibrosis and associated with increased stress kinase activation and apoptosis. Histological and serological improvement after interleukin-10 therapy was accompanied by normalization of keratin hyperphosphorylation on some sites in 7 of 10 patients. In conclusion, site-specific keratin phosphorylation in liver disease is a progression marker when increased and a likely regression marker when decreased. Copyright 2004 American Association for the Study of Liver Diseases
PMID: 15368451 [PubMed - indexed for MEDLINE]

31: Hepatology. 2004 Aug;40(2):327-34.
Haplotype-tagging RANTES gene variants influence response to antiviral therapy in chronic hepatitis C.
Wasmuth HE, Werth A, Mueller T, Berg T, Dietrich CG, Geier A, Gartung C, Lorenzen J, Matern S, Lammert F.
Department of Medicine III, University Hospital Aachen, Aachen University, Aachen, Germany.
The response to antiviral therapy for chronic hepatitis C virus (HCV) is complex and is determined by both environmental and genetic factors. Recently, interacting gene polymorphisms of the chemokine RANTES have been shown to affect HIV disease progression. Our aim was to assess if these RANTES variants are associated with response to anti-HCV therapy. Three linked RANTES single nucleotide polymorphisms (403 G/A, Int1.1 T/C, and 3' 222 T/C) were determined in 297 Caucasian patients who were treated for chronic HCV infection and 152 control subjects. Characteristic nucleotide combinations on single chromosomes (haplotypes) were reconstructed and tested for disease association. Four common RANTES haplotypes (prevalence 73%) were identified in patients and controls. There was a strong association of RANTES haplotype distribution with outcome of antiviral combination therapy (P = .007). Specifically, RANTES haplotypes carrying Int1.1 C and 3' 222 C alleles were more frequent in nonresponders than in patients with a sustained response to antiviral therapy (odds ratio 1.9, P =.01). The influence of these RANTES haplotypes on the outcome of therapy was more pronounced in patients infected with HCV genotypes 1 and 4 (odds ratio 2.3, P = .02). Because RANTES haplotypes carrying Int1.1 C are known to down-regulate RANTES transcriptional activity in vitro, the haplotype analysis fits the hypothesis of a diminished T helper 1 lymphocyte response in patients with a negative response to antiviral therapy. In conclusion, RANTES haplotypes might contribute to the polygenic interaction between HCV and the host immune system and could help to risk stratify patients prior to antiviral therapy. Copyright 2004 American Association for the Study of Liver Diseases
PMID: 15368437 [PubMed - indexed for MEDLINE]

32: Hepatology. 2004 Aug;40(2):289-99.
Antiviral CD8-mediated responses in chronic HCV carriers with HBV superinfection.
Boni C, Amadei B, Urbani S, Fisicaro P, Zerbini A, Mori C, Missale G, Bertoni R, Azzurri A, Del Prete G, Ferrari C.
Divisione Malattie Infettive ed Epatologia (Division of Infectious Diseases and Hepatology), Azienda Ospedaliera Universitaria di Parma, Parma, Italy.
Hepatitis B virus (HBV) superinfection in chronic hepatitis C represents a natural model to investigate whether or not hepatitis C virus (HCV) can influence priming and maturation of antiviral T cells; whether or not HBV superinfection, which is known to determine control of HCV replication, can restore HCV-specific T cell responsiveness; and whether or not cytokines stimulated by HBV infection can contribute to HCV control. To address these issues, the function of CD8 cells specific for HBV and HCV was studied longitudinally in two chronic HCV

patients superinfected with HBV. Patients with acute hepatitis B were also examined. Frequency and function of HBV tetramer+CD8 cells were comparable in patients acutely infected with HBV with or without chronic HCV infection. HBV-specific CD8 cell function was efficiently expressed
irrespective of serum HCV-RNA levels. Moreover, fluctuations of HCV viremia at the time of HBV superinfection were not associated with evident changes of CD8 responsiveness to HCV. Finally, no correlation was found between serum levels of interferon alpha, interleukin (IL)-12, IL-10, or IL-18 and control of HCV replication. In conclusion, HCV did not affect the induction of primary and memory HBV-specific CD8 responses. HCV-specific CD8 responses were undetectable when HCV-RNA was negative, showing that inhibition of HCV replication in the setting of a HBV superinfection was not sufficient to induce a restoration of CD8 reactivity against HCV. Copyright 2004 American Association for the Study of Liver Diseases
PMID: 15368433 [PubMed - indexed for MEDLINE]

33: J Clin Endocrinol Metab. 2004 Sep;89(9):4325-30.
Osteoporosis, mineral metabolism, and serum soluble tumor necrosis factor receptor p55 in viral cirrhosis.
Gonzalez-Calvin JL, Gallego-Rojo F, Fernandez-Perez R, Casado-Caballero F, Ruiz-Escolano E, Olivares EG.
Department of Gastroenterology, University Hospital San Cecilio, 18012 Granada, Spain. jorgegonzalezc@meditex.es
Liver cirrhosis is a risk factor for osteoporosis. Nevertheless, little is known about the mechanisms of bone mass loss in patients with viral cirrhosis. TNFalpha is a potent bone-resorbing agent. Serum concentrations of soluble TNF receptor p55 (sTNFR-55) correlate with clinical activity in liver cirrhosis. Our aim was to evaluate the possible role of sTNFR-55 in the pathogenesis of osteoporosis in patients with viral cirrhosis and its relationship with bone turnover markers. We studied 40 consecutive patients with viral cirrhosis and no
history of alcohol intake and 26 healthy volunteers. Bone mineral density (BMD)
was measured by dual x-ray absorptiometry in the lumbar spine (LS) and femoral
neck (FN). Patients with viral cirrhosis had reduced BMD (expressed as the z-score) in all sites [LS, -1.5 +/- 0.22 ($P < 0.001$); FN, -0.37 +/- 0.15 ($P < 0.01$)]. Serum concentrations of sTNFR-55 and urinary deoxypyridinoline, a biochemical marker of bone resorption, were significantly higher in patients with osteoporosis than in patients without osteoporosis ($P < 0.001$ and $P < 0.05$, respectively). Serum levels of sTNFR-55 correlated inversely with BMD in LS ($r =$
-0.62; $P < 0.005$) and FN ($r = -0.47$; $P < 0.05$) and positively with urinary deoxypyridinoline ($r = 0.72$, $P < 0.001$). Our findings show that high serum concentrations of sTNFR-55 play a role in the pathogenesis of viral cirrhosis-associated bone mass loss and provide evidence of increased bone resorption related to the high serum sTNFR-55 levels.
PMID: 15356028 [PubMed - indexed for MEDLINE]

34: J Clin Microbiol. 2004 Aug;42(8):3904-5.
Two novel clinical presentations of Burkholderia cepacia infection.
Mukhopadhyay C, Bhargava A, Ayyagari A.
Department of Microbiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebarely Rd., Lucknow, U.P., Pin 226014, India.
We report two cases of multidrug-resistant Burkholderia cepacia (B. cepacia genomovar I) and Burkholderia multivorans causing multiple liver abscesses in a patient with bronchial asthma (case 1) and peritonitis in a patient with cirrhosis and hepatitis C virus disease (case 2), respectively. Both patients were treated successfully.
Publication Types:
Case Reports
PMID: 15297563 [PubMed - indexed for MEDLINE]

35: J Clin Pathol. 2004 Aug;57(8):867-71.
Microvessel density and clinicopathological characteristics in hepatitis C virus and hepatitis B virus related hepatocellular carcinoma.
Messerini L, Novelli L, Comin CE.
Department of Human Pathology and Oncology, University of Florence Medical School, Viale G.B. Morgagni, 85, 50134 Florence, Italy.
AIMS: To compare intratumorous microvessel density (MVD) and clinicopathological features in two different groups of hepatocellular carcinoma (HCC), namely: hepatitis B virus (HBV)

related HCC (B-HCC) and HCV related HCC (C-HCC). METHODS: Fifty consecutive cases each of B-HCC and of C-HCC were studied. Microvessel numbers were assessed by staining for the antigen CD34; in each case, three areas with the highest numbers of microvessels were counted in both the intratumorous and the surrounding non-tumorous tissue; the mean value represented the final MVD. RESULTS: Patients with B-HCC were significantly younger than those with C-HCC (mean age, 60.1 (SD, 4.1) v 66.4 (4.3) years); no significant differences were seen for sex or Child's class distribution. The tumour diameter was larger in B-HCCs than in C-HCCs (mean, 5.6 (SD, 1.8) v 3.8 (1.8) cm). Tumour microsatellite formation was significantly higher in C-HCCs (12 v 4 cases). No differences were found for histological subtype, degree of
differentiation, tumour encapsulation, and vascular invasion. The mean MVD value was significantly higher in tumorous (mean, 54 (SD, 13.8) v 38 (8.9)) and in the surrounding non-tumorous liver tissue (mean, 15 (SD, 4.3) v 7 (3.1)) of C-HCCs. CONCLUSIONS: C-HCCs present as smaller tumours in older patients, with a higher incidence of tumour microsatellite formation and higher MVD values both in the tumorous and the non-tumorous areas, suggesting a link between HCV infection, angiogenesis, and hepatocarcinogenesis.
PMID: 15280410 [PubMed - indexed for MEDLINE]

36: J Egypt Soc Parasitol. 2004 Aug;34(2):483-500.
DNA ploidy and S-phase fraction in the patients of chronic HCV and hepatocellular carcinomas.
Sanad SM, Mangoud AM, Shalabi AA, Saber M, Fouad MA.
Department of Zoology, Faculty of Science, Zagazig University, Egypt.
Four hundred blue Fulgen-stained nuclei were measured from each lesion by using DNA image cytometry. The histopathological and cytopathological observations revealed that (52 cases, 69.3%) had a variable degrees of chronic hepatitis, (12cases 16 %) were emerging into cirrhosis, while (11 cases 14.7%) represented different grades of HCC. Most of the cases with minimal or mild chronic hepatitis were female, while most of male had moderate or severe chronic hepatitis, cirrhosis and HCC. DNA image analysis data gave the support of to the histological observations. All of chronic hepatitis C and cirrhotic cases showed normal diploid and/or tetraploid histograms, although increasing S-phase fraction s' values of the highly diseased chronic hepatitis and cirrhotic cases. Hepatocellular carcinomas and one cirrhotic case only revealed aneuploidy (diploid and tetraploid), while one case of poorly differentiated HCC revealed multiploid histogram. So, histopathological severity in cases of progressive chronic hepatitis seems to be associated with the age and sex of Egyptian society. Also, demonstrates the potential usefulness of image cytometry for the evaluation of the different histopathological problems.
PMID: 15287172 [PubMed - indexed for MEDLINE]

37: J Egypt Soc Parasitol. 2004 Aug;34(2):383-95.
Non-histological assessment of liver fibrosis in HCV infection.
Mangoud AM, Sanad SM, Hendawy A, el-Hady G, el-Sherbiny GT.
Early Cancer Detection Unit, Faculty of Medicine, Zagazig University, Egypt.
This study found a correlation between some serum markers [AST/ALT ratio, level of matrix metalloproteinase 9 (MMP9), level of viraemia and HCV serotype] and severity of liver fibrosis in HCV-infected patients. The study included 72 human cases referred to the Early Cancer Detection Unit, for liver biopsy assessment. The severity of liver fibrosis was staged using the METAVIR scoring system into 4 stages. The level of viraemia did not differ significantly in the different stages of liver fibrosis. Also, the type of HCV had no effect on the severity of liver fibrosis. However, the transaminases ratio differed significantly in the different fibrosis stages ($P < 0.01$). This serum test has a relatively high sensitivity and specificity (92.6% and 94.3%, respectively) in diagnosing severe fibrosis and cirrhosis. The level of MMP9 was, however, inversely correlated with the fibrosis stages and was found to have an 88.9% sensitivity and an 88.6% specificity when diagnosing severe fibrosis and cirrhosis. Although, the sensitivity of these serum markers did not reach 100%, yet their use can reduce the number of liver biopsies when diagnosing and treating HCV-infected patients.
PMID: 15287165 [PubMed - indexed for MEDLINE]

38: J Gen Virol. 2004 Sep;85(Pt 9):2515-23.
Expression of hepatitis C virus proteins in epithelial intestinal cells in vivo.
Deforges S, Evlashev A, Perret M, Sodoyer M, Pouzol S, Scoazec JY, Bonnaud B, Diaz O, Paranhos-Baccala G, Lotteau V, Andre P.
INSERM U503, IFR128 Biosciences Lyon Gerland, 21 avenue Tony Garnier, 69365 Lyon

cedex 07, France.
Previous work on hepatitis C virus (HCV) led to the discovery of a new form of virus particle associating virus and lipoprotein elements. These hybrid particles (LVP for lipo-viro-particles) are enriched in triglycerides and contain at least apolipoprotein B (apoB), HCV RNA and core protein. These findings suggest that LVP synthesis could occur in liver and intestine, the two main organs specialized in the production of apoB-containing lipoprotein. To identify the site of LVP production, the genetic diversity and phylogenetic relationship of HCV quasispecies from purified LVP, whole serum and liver biopsies from chronically infected patients were studied. HCV quasispecies from LVP and liver differed significantly, suggesting that LVP were not predominantly synthesized in the liver but might also originate in the intestine. The authors therefore searched for the presence of HCV in the small intestine. Paraffin-embedded intestinal biopsies from 10 chronically HCV-infected patients and from 12 HCV RNA-negative controls (10 anti-HCV antibody-negative and two anti-HCV antibody-positive patients) were tested for HCV protein expression. HCV NS3 and NS5A proteins were stained in small intestine epithelial cells in four of the 10 chronically infected patients, and not in controls. Cells expressing HCV proteins were apoB-producing enterocytes but not mucus-secreting cells. These data indicate that the small intestine can be infected by HCV, and identify this organ as a potential reservoir and replication site. This further emphasizes the interaction between lipoprotein metabolism and HCV, and offers new insights into hepatitis C infection and pathophysiology.
PMID: 15302945 [PubMed - indexed for MEDLINE]

39: J Immunol. 2004 Sep 1;173(5):3549-56.
Frequent joining of Bcl-2 to a JH6 gene in hepatitis C virus-associated t(14;18).
Sasso EH, Martinez M, Yarfitz SL, Ghillani P, Musset L, Piette JC, Cacoub P.
Department of Medicine, University of Washington, Seattle 98105, USA.
eric.sasso@abbott.com
The t(14;18) chromosomal translocation, which joins the Bcl-2 proto-oncogene to an Ig J(H) gene, has increased prevalence in patients chronically infected with hepatitis C virus (HCV). We now establish a link between the molecular structure and clinical occurrence of HCV-associated t(14;18). A t(14;18) was detected by PCR in leukocytes from 22 of 46 HCV-infected patients (48%) and 11 of 54 healthy controls (20%) ($p = 0.0053$). Nucleotide sequence analysis of the Bcl-2/J(H) joins found a J(H)6 gene in 18 of 22 (82%) t(14;18) from HCV(+) patients, and 3
of 8 (38%) from controls ($p = 0.031$). The t(14;18) rarely contained J(H) gene mutations, or an intervening region sequence suggestive of D gene rearrangement or templated nucleotide insertion. Analysis of published t(14;18) nucleotide sequences established that the J(H)6 prevalence in t(14;18) from normal/nonneoplastic controls (48%) was significantly lower than in t(14;18) from our HCV(+) patients ($p = 0.004$) or from non-Hodgkin's lymphomas (66%, $p =$
0.003). We conclude that the increased prevalence of t(14;18) in HCV(+) patients occurs with a strong bias for Bcl-2/J(H)6 joins. In this regard, HCV-associated t(14;18) more closely resemble t(14;18) in lymphomas than t(14;18) from normal subjects.
PMID: 15322220 [PubMed - indexed for MEDLINE]

40: J Infect Dis. 2004 Sep 15;190(6):1199-200; author reply 1200-1.
Comment on:
J Infect Dis. 2004 Jan 15;189(2):292-302.
Changes in the prevalence of hepatitis C virus genotype among injection drug users: a highly dynamic process.
Schroter M, Zollner B, Laufs R, Feucht HH.
Publication Types:
Comment
Letter
PMID: 15319872 [PubMed - indexed for MEDLINE]

41: J Infect Dis. 2004 Sep 15;190(6):1098-108. Epub 2004 Aug 10.
Viral gene sequences reveal the variable history of hepatitis C virus infection among countries.
Nakano T, Lu L, Liu P, Pybus OG.
Department of Internal Medicine, Ichinomiya Nishi Hospital, Okucho Orikuchinishi 89-1, Ichinomiya, Aichi 491-0201, Japan. nakano@anzu.or.jp
BACKGROUND: The analysis of molecular phylogenies estimated from the gene sequences of sampled viruses can provide important insights into epidemiological processes. METHODS: The

demographic and migration histories of the prevalent hepatitis C virus (HCV) subtypes 1a and 1b were inferred from viral gene sequences sampled in 5 countries. Estimated viral phylogenies were analyzed by use of methods based on parsimony and coalescent theory. RESULTS: The parsimony migration analysis suggested that the global subtype 1a and 1b epidemics are
geographically structured, with asymmetrical movement of HCV strains among the sampled countries. The coalescent analysis indicated that subtype 1a infections in the United States, Brazil, and Indonesia began to increase exponentially during the 1940s and 1950s, whereas in Vietnam the increase began after the 1970s. In contrast, subtype 1b infections in these 4 countries and in Japan began to increase exponentially between 1880 and 1920, with a possible recent decrease in infection rates in Indonesia and Japan. In the United States, Brazil, and Vietnam, the epidemic growth rates for subtype 1a strains were higher than those for subtype 1b strains, whereas the growth rates were similar in Indonesia. CONCLUSIONS: The estimated histories of migration and population growth indicated that patterns of HCV transmission differ among countries and viral subtypes.
PMID: 15319860 [PubMed - indexed for MEDLINE]

42: J Infect Dis. 2004 Sep 15;190(6):1093-7. Epub 2004 Aug 10.
Prevalence of production of virus-specific interferon-gamma among seronegative hepatitis C-resistant subjects reporting injection drug use.
Freeman AJ, Ffrench RA, Post JJ, Harvey CE, Gilmour SJ, White PA, Marinos G, van Beek I, Rawlinson WD, Lloyd AR.
Department of Pathology, School of Medical Sciences, The University of New South Wales, Sydney, New South Wales, Australia. freemanto@sesahs.nsw.gov.au
This report describes subjects who were highly likely to have been repeatedly exposed to hepatitis C virus (HCV) through injection drug use and who remained negative for anti-HCV antibody. Production of virus-specific interferon- gamma by peripheral blood mononuclear cells was seen in the majority of subjects (72%) and was associated with higher-risk behavior. For 92% of the subjects, results of recombinant immunoblot assays demonstrated faint bands against nonstructural proteins. The immune responses described are likely to have been primed and maintained by episodes of subclinical infection without classic seroconversion and may indicate a hepatitis C-resistant phenotype. Vaccine strategies to mimic this response may provide protection against persistent HCV infection.
PMID: 15319859 [PubMed - indexed for MEDLINE]

43: J Infect Dis. 2004 Sep 1;190(5):989-97. Epub 2004 Jul 23.
Expression of chemokine receptors on intrahepatic and peripheral lymphocytes in chronic hepatitis C infection: its relationship to liver inflammation.
Wang J, Holmes TH, Cheung R, Greenberg HB, He XS.
Stanford University School of Medicine, California, USA.
BACKGROUND: Intrahepatic lymphocytes are believed to be directly involved in the immunopathogenesis of chronic liver diseases. Little is known about the trafficking of lymphocytes into the liver and their role in chronic hepatitis C infection. METHODS: The expression of 4 chemokine receptors and an activation marker on multiple lymphocyte subsets in paired liver biopsy and peripheral blood specimens from 23 patients with chronic hepatitis C infection were analyzed by a 6-color flow-cytometric assay. RESULTS: CCR5, CXCR3, and CXCR6 were expressed on intrahepatic CD4+ and CD8+ T cells, natural killer (NK) T
cells, NK cells, and B cells at significantly higher frequencies than on peripheral lymphocyte subsets. The expression of these receptors and the activation marker CD38 tended to increase with the severity of liver inflammation. This increase was significant for several intrahepatic lymphocytes subsets. Correlations in expression differed among pairs of these extralymphoid homing receptors on the intrahepatic T cells. CONCLUSIONS: The homing program for intrahepatic lymphocytes involves multiple extralymphoid chemokine receptors that are regulated by >1 pathway. The expression of homing receptors on intrahepatic lymphocytes is associated with the immunopathogenesis of chronic hepatitis C disease. These preliminary results indicate that conformational studies with larger sample sizes are warranted.
PMID: 15295707 [PubMed - indexed for MEDLINE]

44: J Infect Dis. 2004 Aug 15;190(4):819-25. Epub 2004 Jul 16.
Iron regulates hepatitis C virus translation via stimulation of expression of translation initiation factor 3.
Theurl I, Zoller H, Obrist P, Datz C, Bachmann F, Elliott RM, Weiss G.

Department of Internal Medicine, University of Innsbruck, Innsbruck, Austria.
BACKGROUND: Although the response to treatment with interferon- alpha in individuals with chronic hepatitis C virus (HCV) infection is negatively associated with increased liver iron stores, the underlying mechanisms at work have remained elusive to date. The translation initiation factor 3 (eIF3) is essential for HCV translation, and thus the effects that iron perturbations have
on eIF3 expression and HCV translation were studied here. METHODS: eIF3 expression was analyzed by TaqMan polymerase chain reaction, Northern and Western blot analysis of HepG2 cells, and liver biopsies. Functional effects of iron on HCV mRNA translation were estimated by use of transient transfection experiments with bicistronic vectors. RESULTS: Iron treatment of HepG2 cells increased eIF3 mRNA and protein expression, whereas iron chelation reduced it. Accordingly, iron-dependent stimulation of eIF3 specifically induced the expression of reporter genes under the control of regulatory HCV mRNA stem-loop structures. Moreover, a positive association between liver iron levels, eIF3 expression, and HCV expression was found when liver-biopsy samples from HCV-infected patients were analyzed. CONCLUSION: Iron promotes the translation of HCV by stimulating the expression of eIF3, which may be one reason for the negative association between liver iron overload and HCV infection. Modulation of the affinity of eIF3 to bind to HCV mRNA may be a promising target for the treatment of chronic HCV infection.
PMID: 15272411 [PubMed - indexed for MEDLINE]

45: J Trop Pediatr. 2004 Aug;50(4):236-8.
Mother-to-Infant transmission of hepatitis C virus (HCV) in Brazil.
Lima MP, Pedro RJ, Rocha MD.
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Sixty-one women with anti-HCV antibodies, detected by a third-generation enzyme immunoassay (EIA3), were prospectively recruited for investigation of vertical HCV transmission during child-birth, at the University Hospital of the Catholic University of Campinas, Brazil, between January 1994 and July 1998. Six of the women presented coinfection with the human immunodeficiency virus type 1 (HIV-1). All of the 72 children born in this period were followed at least until they were 18 months of age. Analyses of anti-HCV, HCV RNA, and alanine
aminotransferase were performed in a minimum of two blood samples during follow-up. One (2.4 per cent; 95 per cent CI, 2.2-7) of the 42 children born to HCV viremic mothers was both anti-HCV and HCV RNA-positive, with altered ALT levels. Passively transferred maternal anti-HCV antibodies became undetectable within 9-12 months. None of the nine infants born to HIV-1 infected mothers were infected either by HIV or HCV. Thus, the mother-infant HCV transmission rate is low and seems to be associated with maternal HCV RNA positivity.
PMID: 15357565 [PubMed - indexed for MEDLINE]

46: J Virol. 2004 Sep;78(18):9782-9.
Long-term persistence of infection in chimpanzees inoculated with an infectious hepatitis C virus clone is associated with a decrease in the viral amino acid substitution rate and low levels of heterogeneity.
Fernandez J, Taylor D, Morhardt DR, Mihalik K, Puig M, Rice CM, Feinstone SM, Major ME.
Laboratory of Hepatitis Viruses, Division of Viral Products, Center for Biologics Evaluation and Research, Food and Drug Administration, Building 29A, Room 1D10, HVM 448, 8800 Rockville Pike, Bethesda, MD 20892, USA.
Two chimpanzees, 1535 and 1536, became persistently infected following inoculation with RNA transcripts from cDNA clones of hepatitis C virus (HCV). Analysis of the HCV genomes from both animals showed an accumulation of amino acid substitutions over time. The appearance of substitutions in the envelope genes was associated with increased antienvelope antibody titers. However, extensive mutations were not incorporated into hypervariable region 1 (HVR1). A
comparison of the nonsynonymous substitution rate/synonymous substitution rate was made at various time points to analyze selective pressure. The highest level of selective pressure occurred during the acute phase and decreased as the infection continued. The nonsynonymous substitution rate was initially higher than the synonymous substitution rate but decreased over time from 3.3 x 10(-3) (chimpanzee 1535) and 3.2 x 10(-3) (chimpanzee 1536) substitutions/site/year at week 26 to 1.4 x 10(-3) (chimpanzee 1535) and 1.7 x 10(-3) (chimpanzee 1536) at week 216, while the synonymous substitution rate remained steady at

approximately 1 x 10(-3) substitutions/site/year. Analysis of PCR products using single-stranded conformational polymorphism indicated a low level of heterogeneity in the viral genome. The results of these studies confirm that the persistence of infection is not solely due to changes in HVR1 or heterogeneity and that the majority of variants observed in natural infections could not arise simply through mutation during the time period most humans and chimpanzees are
observed. These data also indicate that immune pressure and selection continue throughout the chronic phase. Copyright 2004 American Society for Microbiology
PMID: 15331711 [PubMed - indexed for MEDLINE]

47: J Virol. 2004 Sep;78(17):9030-40.
Inhibition of hepatitis C virus-like particle binding to target cells by antiviral antibodies in acute and chronic hepatitis C.
Steinmann D, Barth H, Gissler B, Schurmann P, Adah MI, Gerlach JT, Pape GR, Depla E, Jacobs D, Maertens G, Patel AH, Inchauspe G, Liang TJ, Blum HE, Baumert TF.
Department of Medicine II, University of Freiburg, Freiburg, Germany.
Hepatitis C virus (HCV) is a leading cause of chronic viral hepatitis worldwide. The study of antibody-mediated virus neutralization has been hampered by the lack of an efficient and high-throughput cell culture system for the study of virus neutralization. The HCV structural proteins have been shown to assemble into noninfectious HCV-like particles (HCV-LPs). Similar to serum-derived virions, HCV-LPs bind and enter human hepatocytes and hepatoma cell lines. In
this study, we developed an HCV-LP-based model system for a systematic functional analysis of antiviral antibodies from patients with acute or chronic hepatitis C. We demonstrate that cellular HCV-LP binding was specifically inhibited by antiviral antibodies from patients with acute or chronic hepatitis C in a dose-dependent manner. Using a library of homologous overlapping envelope peptides covering the entire HCV envelope, we identified an epitope in the N-terminal E2 region (SQKIQLVNTNGSWHI; amino acid positions 408 to 422) as one target of human antiviral antibodies inhibiting cellular particle binding. Using a large panel of serum samples from patients with acute and chronic hepatitis C, we demonstrated that the presence of antibodies with inhibition of binding activity was not associated with viral clearance. In conclusion, antibody-mediated inhibition of cellular HCV-LP binding represents a convenient
system for the functional characterization of human anti-HCV antibodies, allowing the mapping of envelope neutralization epitopes targeted by naturally occurring antiviral antibodies.
PMID: 15308699 [PubMed - indexed for MEDLINE]

48: Lancet. 2004 Aug 28;364(9436):757-8; author reply 758.
Comment on:
Lancet. 2003 Nov 22;362(9397):1708-13.
Lancet. 2004 Feb 14;363(9408):570; author reply 571.
HIV/HCV coinfection, HAART, and liver-related mortality.
Sabin CA, Walker AS, Dunn D.
Publication Types:
Comment
Letter
PMID: 15337398 [PubMed - indexed for MEDLINE]

49: Lancet Infect Dis. 2004 Oct;4(10):605.
Comment on:
Lancet Infect Dis. 2004 May;4(5):253.
Injecting reason.
Sharpe R.
Common Sense for Drug Policy, Washington, DC 20012, USA. rsharpe@csdp.org <rsharpe@csdp.org>
Publication Types:
Comment
PMID: 15451484 [PubMed - indexed for MEDLINE]

50: South Med J. 2004 Sep;97(9):890-3.

Desquamative interstitial pneumonia and hepatitis C virus infection: a rare association.
Iskandar SB, McKinney LA, Shah L, Roy TM, Byrd RP Jr.
The Veterans Affairs Medical Center, Mountain Home, TN 37684-4000, USA.
Extrahepatic manifestations of hepatitis C virus (HCV) infection are common. The authors report the unusual occurrence of desquamative interstitial pneumonia (DIP) in a patient with HCV. An immunologic response to HCV Infection may have a role in the pathogenesis of DIP in patients with chronic HCV. Since DIP is treatable, HCV patients with pulmonary infiltrates should be thoroughly investigated for this disorder. In our experience, the use of steroids in HCV-associated DIP improved the patient's respiratory status without increasing the viral load.
Publication Types:
Case Reports
Review
Review of Reported Cases
PMID: 15455981 [PubMed - indexed for MEDLINE]

51: Transfusion. 2004 Sep;44(9):1344-9.
Hepatitis C seroprevalence in accepted versus deferred blood-donor candidates evaluated by medical history and self-exclusion form.
Lopez RA, Romero-Estrella S, Infante-Ramirez L, Mendez-Aquino JS, Berron-Ruiz P, Morales-Alfaro NA, Vivar R, Carrada E, Rivera-Rendon Mdel R, Sanchez-Guerrero SA.
National Center for Blood Transfusion, Mexico City, Mexico.
BACKGROUND: Hepatitis C virus (HCV) represents a viral pandemic that is five times as widespread as human immunodeficiency virus. Blood transfusion posed a major risk of HCV infection in developed countries before 1990, but the introduction of improved blood-screening measures has decreased the risk of transfusion-associated HCV infection, which may now be even lower since the introduction of screening of pooled samples by nucleic acid testing (NAT). Unfortunately, NAT is not affordable in most developing countries. The goal of this work is to assess the usefulness of both screening measures, the medical history, and the self-exclusion form to distinguish between high-risk and low-risk populations of HCV-carrier blood-donor candidates in Mexico. STUDY DESIGN AND METHODS: From February 2002 to April 2003, 4174 consecutive candidates were enrolled in a prospective, nonrandomized and comparative study. In total, 4158 candidates were included in the analysis and divided in two groups: Group A consisted of 3101 accepted donors and Group B consisted of 1057 deferred donors according to a complete medical history and self-exclusion form. The only exclusion criteria was the lack of a signed consent form to enter the study. All candidates from both groups underwent anti-HCV detection by third-generation enzyme immunoassay (EIA). Those who had either a positive or gray-zone signal-to-cutoff ratio underwent polymerase chain reaction and a second EIA test. If the second EIA test resulted in either a positive or gray-zone signal-to-cutoff ratio, a recombinant immunoblot assay test was performed. The chi-square test was used for statistical analysis, and a p value less than 0.05 was considered significant. RESULTS: Anti-HCV prevalence by the EIA method was as follows: 0.61 percent for Group A and 1.32 percent for Group B ($p = 0.0243$); whereas with recombinant immunoblot assay the prevalence was 0.19 percent for Group A and 0.47 percent for Group B ($p = 0.1265$). When we analyzed the polymerase chain reaction test results, the prevalence in Group A was 0.10 percent (95% confidence interval, 0.089-0.110) and in Group B was 0.47 percent (95% confidence interval, 0.439-0.500) ($p = 0.0159$). CONCLUSIONS: The medical history of blood donors in conjunction with serologic screening tests helps to improve blood transfusion safety. This measure is recommended in blood banks of those countries where NAT is still unaffordable.
Publication Types:
Clinical Trial
Controlled Clinical Trial
PMID: 15318859 [PubMed - indexed for MEDLINE]

52: Transplantation. 2004 Aug 27;78(4):580-3.
Hepatitis C virus infection with hepatocellular carcinoma: not a controversial indication for liver transplantation.
Rodriguez-Luna H, Balan V, Sharma P, Byrne T, Mulligan D, Rakela J, Vargas HE.
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BACKGROUND: The association of hepatocellular carcinoma (HCC) and chronic hepatitis C virus (HCV) infection has been identified as a potential contraindication for orthotopic liver transplantation (LT) because of lower survival rate compared with other indications. AIM: Evaluate the outcome of patients with and without HCC and cirrhosis with and without chronic HCV infection undergoing transplantation. Determine the postLT HCC recurrence rate and frequency of de novo postLT HCC. PATIENTS AND METHODS: United Network for Organ Sharing (UNOS) data was collected from January 1998 to December 2002. Cohort included 17,968 patients (11,552 M; 6,416 F) with a mean age of 51 (18-87) years. Four groups were established: HCV (n = 7,079), HCC (n = 611), HCV+HCC (n = 1,078), and no HCV/no HCC (n = 9,200). The overall survival rate was calculated at 24 and 48 months postLT. RESULTS: Patient survival at 24 months and 48 months was 84% and 75% for HCV, 84% and 68% for HCC, 78% and 72% for HCV+HCC, and 85% and 80% for no HCV/no HCC, respectively. Survival at 48 months among the two groups was not significantly different (NS). Further analysis of these groups revealed a statistically significant advantage in survival at 48 months postLT for the no HCV/no HCC group when compared with the HCV group.($P < 0.05$) The reported rate of postLT HCC recurrence and de novo postLT HCC was 3.3% and 0.05%, respectively. CONCLUSION: In this large cohort of U.S. patients, HCC does not have an impact on the survival of LT patients infected with HCV.
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